After the line beginning "Fac7" and ending "PRPGVLLRAP FP", please insert --(SEQ ID No: 7)--.

Please amend Figure 2 as follows:

After the line ending "R D W I K E N T G V", please insert --(SEQ ID No: 2)--

After the line "3121

Please amend Figure 3 by inserting --(SEQ ID No: 2)--after the line "851 ENTGV".

Please amend Figure 11 as follows: In the line beginning "hTADG15 ENTGV*" and ending "900", after "ENTGV*", please insert --(SEQ ID No: 2)--.

In the line consisting of "mEpithin HP", after "HP" please insert --(SEQ ID No: 10)--.

Please amend Figure 12 as follows:

On the bottom of page 1, please replace FIGURE 12-1 with --Figure 12--

On page 2, after the line ending "3147", please insert --(SEQ ID No: 1)--.

On page 2, after the line ending "2900", please insert --(Seq ID No: 9)--.

On the bottom of page 2, please replace FIGURE 12-2 with --Figure 12 (continued)--

REMARKS

Objections to the Oath or Declaration

A replacement Combined Declaration and Power of Attorney is enclosed herewith. The Applicants respectfully request that the objection to the oath or declaration be withdrawn.

Objections to the Drawings

The drawings are objected to for various informalities. Figures 1. 2. 3, 11 and 12 have been amended herein. The changes to the figures are indicated in red on the enclosed copies and have only been made to introduce sequence identifiers into Figures 1, 2, 3, 11 and 12. Formal drawings will be submitted upon acceptance of the instant application.

Objections to the Specification

The abstract has been objected to for not making reference to the claimed invention. This objection is respectfully traversed. The abstract has been amended to include the sentence -- The instant invention also includes a kit containing antibodies for the detection of TADG-15 protein.-- Since, as amended, the abstract describes the instant invention, the Applicants respectfully request that the objection to the abstract be withdrawn.

The title has been objected to as not descriptive. This objection is respectfully traversed. The title has been amended herein. Therefore, the Applicants respectfully request that the objection to the title be withdrawn.

The disclosure has been objected to because the brief description of the figures lacks separate descriptions of Figures 12-1 and 12-2. This objection is respectfully traversed.

Figure 12 is improperly labeled as Figure 12-1 and 12-2. Figures 12-1 and 12-2 simply refer to the first and second pages of the same figure. Figure 12 has been amended herein to replace "Figure 12-1" with --Figure 12-- and "Figure 12-2" with --Figure 12 (continued)--. These changes are indicated in red on the enclosed copy of Figure 12. As such, the brief description of the figures is correct as is. Therefore, the applications respectfully request that this objection to the disclosure be withdrawn.

The 35 USC §112 Rejection

Claims 22-24 stand rejected under 35 USC §112, second paragraph, as indefinite. This rejection is respectfully traversed.

First of all, the Examiner states that the recitation "TADG-15" in claims 22 and 24 is vague and indefinite. Therefore, claims 22 and 24 have been amended herein to include the full name of the protein, i.e. Tumor Antigen Derived Gene-15. The Examiner also states that the recitations "fragment thereof" in claims 22 and 24 is vague and indefinite. Therefore, amendments

have been made herein to delete this recitation from claims 22 and 24. As amended, claims 22 and 24 are no longer vague and indefinite. Therefore, the Applicants respectfully request that the 35 USC \$112, second paragraph, rejection of claims 22-24 as indefinite be withdrawn.

The 35 U.S.C. §103 Rejections

Claims 22-24 stand rejected under 35 U.S.C. §103(a), as unpatentable over GenBank Accession Number W22987 (October 8, 1997), in view of Lerner (Nature 299:592-596, 1982). This rejection is respectfully traversed.

W22987 describes the sequence of a serine protease expressed in the human colon carcinoma cell line COLO 201. serine protease is identical to amino acids 615-855 of TADG-15. Lerner describes methods of generating antibodies predetermined specificity to various antigens. The Examiner contends that it would be obvious to use the teachings of Lerner to generate an antibody against all or part of W22987 to obtain an antibody against TADG-15 to incorporate into the kit of the instant invention. The Applicants respectfully disagree.

Claims 22 and 24 explicitly state that the antibody in the kit is "specific for TADG-15." An antibody raised against W22987 would not fit this criterion. Amino acids 615-815 correspond to the serine protease domain of TADG-15. As evidenced by Figure 1 of the instant specification, this domain is highly homologous number of other known serine proteases. Thus, this would not be the best segment to use to obtain an antibody specific for TADG-15. TADG-15 contains a number of domains which are not present in either W22987 or the other serine proteases of Figure Therefore, given the knowledge that TADG-15 is 100% identical to another known protease starting after residue 615, it would be obvious that an antibody specific for TADG-15 must be generated from amino acid sequences before 615. Also, the Examiner seems to be implying that W22987 is a fragment of TADG-15. However, no evidence or suggestion that this is the case can be gleaned from the combination or W22987 and Lerner. Rather, W22987 the protein as a small, complete protease. However, even if it is a fragment of a larger protease, there is no suggestion that it is a fragment of TADG-15. Therefore, the applicant respectfully requests that the 35 U.S.C. §103(a) rejection of claims 22-24 under

as unpatentable over GenBank Accession Number W22987 in view of Lerner be withdrawn.

This is intended to be a complete response to the Office Action mailed June 29, 2000. If any issues remain outstanding, the Examiner is respectfully requested to telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,

Date: - 1/2000

Benjamin Aaron Adler, Ph.D., J.D.

Registration No. 35,423 Counsel for Applicant

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COMBINED DECLARATION AND POWER OF ATTORNEY

Timothy J. O'Brien and Hirotoshi Tanimoto, as below-named inventors, hereby declare that: our residences, post office address and citizenship are is stated below next to our names; we believe we are the original, first and joint inventors of he subject matter which is claimed and for which a patent is sought on the invention entitled TAL'G-15: An Extracellular Serine Protease Overexpressed in Carcinomas, USSN 09:421,213 filed October 20. 1999.

We hereby state that we have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above. We acknowledge the duty to disclose all information we know to be material to patentability in accordance with Title 37. Code of Federal Regulations, §1.56(a), including information which became known to us between the filing date of the prior application and the national or PCT international filing date of this patent application.

We hereby appoint the following attorneys and/or agents to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith: Dr. Martin L. McGregor, Registration No. 29.239 and Dr. Benjamin Adler, Registration No. 35,423. Address all telephone calls to telephone number 713/777-2321. Address all correspondence to. McGREGOR & ADLER, 8011 Candle Lane, Houston, TX 77071.

We hereby declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

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163-0033 , JAPAN

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Heps RIVGGRDTSL GRWPWQVSL. ....RYDG.A HLCGGSLLSG DWVLTAAHCF PE....RNRV LSRWRVFAGA VAQASPHGLQ
 Tadg15 RVVGGTDADE GEWPWQVSL. .... HALGQG HICGASLISP NWLVSAAHCY IDDRGFRYSD PTQWTAFLGL HDQSQRSAPG
   Scce KIIDGAPCAR GSHPWQVAL. ....LSGNQL H.CGGVLVNE RWVLTAAHC. ...... K MNEYTVHLGS DTLG..DR.R
    Try KIVGGYNCEE NSVPYQVSL. ....NSGYHF ..CGGSLINE QWVVSAGHC. .......Y KSRIQVRLGE HNIEVLEG.N
  Chymb RIVNGEDAVP GSWPWQVSL. ...QDKTGF HFCGGSLISE DWVVTAAHC. ......GV RTSDVVVAGE FDQGSDEE.N Fac7 RIVGGKVCFK GECPWQVLL. ....LVNG.A QLCGGTLINT IWVVSAAHCF DKIKNWRNLI .....AVLGE HDLSEHDGDE
    TDA RIKGGLFADI ASHPWQAAIF AKHRRSPGER FLCGGILISS CWILSAAHCF QERFPPHHL. .... TVILGR .TYRVVPGEE
  Heps LGVQAVVYHG GYLPFRDPNS EENSNDIALV HLSS.PLPLT EYIQPVCLPA ...AGQALVD GKICTVTGWG NTQYYGQQ.A
Tadg15 VQERRLKRII SHPFFNDFTF D...YDIALL ELEK.PAEYS SMVRPICLPD ...ASHVFPA GKAIWVTGWG HTQYGGTG.A
   Scce AQRIKASKSF RHPGYSTQT. ..HVNDLMLV KLNS.QARLS SMVKKVRLPS ...RCE..PP GTTCTVSGWG TTTSPDVTFP
   Try EQFINAAKII RHPQYDRKT. ..LNNDIMLI KLSS.RAVIN ARVSTISLPT ...APP..AT GTKCLISGWG NTASSGADYP
 Chymb IQVLKIAKVF KNPKFSILT. ..VNNDITLL KLAT.PARFS QTVSAVCLPS ...ADDDFPA GTLCATTGWG KTKYNANKTP
  Fac7 QSRRVAQVII P....STYVP GTTNHDIALL RLHQ.FVVLT DHVVPLCLPE RTFSERTLAF VRFSLVSGWG QLLDRGATAL
   Tpa EQKFEVEKYI VHKEFDDDTY D...NDIALL QLKSDSSRCA QESSVVRTVC LPPADLQLPD WTECELSGYG KHEALSPFYS
  Heps GVLQEARWEI ISNDVCNGAD FYGN...QIKP KMFCAGYPEG G......IDA CQGDSGGPFV CEDSISRTPR WRLCGIVSWG
       LILQKGEIRV INQTTCE..N LLPQ..QITP RMMCVGFLSG G.....VDS CQGDSGGPL. ..SSVEADGR IFQAGVVSWG
  Scce SDLMCVDVKL ISPQDCTKV. .YKD..LLEN SMLCAGIPDS K.....KNA CNGDSGGPLV C....R.... GTLQGLVSWG
 Try DELQCLDAPV LSQAKCEAS. .YPG..KITS NMFCVGFLEG G.....KDS CQGDSGGPVV C....N.... GQLQGVVSWG Chymb DKLQQAALPL LSNAECKKS. .WGR..RITD VMICAG..AS G.....VSS CMGDSGGPLV C....QKDGA WTLVGIVSWG
  Fac7 ELMVLNVPRL MTQDCLQQSR KVGDSPNITE YMFCAGYSDG S.....KDS CKGDSGGP....HATHYRGT WYLTGIVSWG
   Tpa ERLKEAHVRL YPSSRCTSQH LLNRT..VTD NMLCAGDTRS GGPQANLHDA CQGDSGGPLV CLN....DGR MTLVGIISWG
 Heps T.GCALAQKP GVYTKVSDFR EWIFQAIKTH SEASGMYTQL ~~ (SEG ID No. 3)
Tadg15 D. GCAQRNKP GVYTRLPLFR DWIKENTGV- ----- -- (SEG 10 No: 2)
 Scce TFPCGQFNDP GVYTQVCKFT KWINDTMKKH R----- -- (SEG 10 No: 4)
  Try . D. GCAQKNKP GVYTKVYNYV KWIKNTIAAN S----- -- (SEQ 10 No: 5)
Chymb SDTCS.TSSP GVYARVTKLI PWVQKILAAN ------ -- (5EG 10 No: 6)
 Fac7 Q.GCATVGHF GVYTRVSQYI EWLQKLMRSE PRPGVLLRAP FP (SEQ 10 No: 7)
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	RLPLERDWIK	AORNKPGVYT	AGVVSWGDGC	COGESCPLS SVEADGRIFO AGVVSWGDGC AORNKPGVYT	COGEGGGEPLS	801
)	VGFLSGGVDS	PQQITPRMMC	INQTTCENLL	GHTQYGGTGA LILQKGEIRV INQTTCENLL PQQITPRMMC	GHTQYGGTGA	751
V	AGKAIWVTGW	CLPDASHVFP	AEYSSMVRPI	PFFNDFTFDY @IALLELEKP AEYSSMVRPI	PFFNDFTFDY	701
	ERRLKRIISH	QSQRSAPGVQ	QWTAFLGLHD	LVSARHCYID DRGFRYSDPT QWTAFLGLHD QSQRSAPGVQ	LVSARACYID	651
,	CGASLISPNW	SLHALGOGHI	ADEGEMPWQV	DCDCGLRSFT ROARVVGGTD ADEGEWPWQV SLHALGQGHI	DCDCGLRSFT	601
	EDCSDCSDEK	SKGNPECDGK	TYRCLNGLCL	GDGSDEASCP KVNVVTCTKH TYRCLNGLCL SKGNPECDGK EDCSDCSDE	GDGSDEASCP	551
4	SOOCNGKDDC	RCSNGKCLSK	QGCSCPAQTE	CKPLFWVCDS VNDCGDNSDE OGCSCPAOTF RCSNGKCLSK	CKPLFWVCDS	501
	GHQFTCKNKF	SDELNCSCDA	CDGWADCTDH	DPCPGQFTCR TGRCIRKELR CDGWADCTDH SDELNCSCDA GHQFTCKNKF	DPCPGQFTCR	451
	LAEYLSYDSS	NSNKITVRFH SDQSYTDTGF LAEYLSYDSS	NSNKITVRFH	GERSQFVVTS	YVEINGEKYĈ	401
	GVPAGTČPKD	SFKFFYLLEP GVPAGTČPKD	EVPNNQHVKV	PPNIDČTWNI	FNSPYYPGHY	351
6	GGRLRKAQGT	* FFQLPRMSSC	ERRHPGFEAT	YNLTFHSSON VLLITLITNT	VNLTFHSSON	301
	VQLČGTYPPS	RSFDLASČDE RGSDLVTVYN TLSPMEPHAL VQLČGTYPPS	RGSDLVTVYN		DADSVLSLTF	251.
	HARČQWALRG	PGFPDSPYPA	RGVELMRFTT	DNSCSFGLHA RGVELMRFTT	TDSKTVQRTQ	201
*	FVVTSVVAFP	IPOHLVEEAE RVMAEERVVM LPPRARSLKS FVVTSVVAFP	RVMAEERVVM	IPOHLVEEAE	VIAYYWSEFS	151
	SAVTAFSEGS	VPFLGPYHKE	KDALKLLYSG	FVDAYENSINS TEFVSLASKV KDALKLLYSG VPFLGPYHKE SAVTAFSEGS	FVDAYENSINS	101
2	NGYMRITNEN	YRDVRVQKVF	GIGFLVGHLQ	GPGRWVVLAA VLIGLLLVIL GIGFLVWHLQ YRDVRVQKVF NGYMRITNEN	GPGRWVVLAA	51
-	VNNVKKVEKH	GLEEGVEFLP	KYNSRHEKVN	MGSDRARKGG GGPKDFGAGL KYNSRHEKVN GLEEGVEFLP VNNVKKVEKH	MGSDRARKGG	

1. Cytoplasmic domain

2. Transmembrane domain

3. CUB repeat

4. Ligand-binding repeat (class A motif) of LDL receptor like domain

Potential Cleavage site Conserved amino acids of catalytic triad II, D, S

NXT: Possible N-linked glycosylation site

: Conserved cysteine residue

5. Serine protease

FIGURE 3

hTADG15 MGSLRARKGG GGPKDFGAGL KYNSRHEKVN GLEEGVEFLP VNNVKKVEKH 50
mapritinN-GASQDL-NMF AAR
hTADG15 GPGRWVVLAA VLIGLLLVLL GIGFLVWHLQ YRDVRVQKVF NGYMRITNEN! 100 i 1841 mEpithinRVFSFLS- MA-LFHNHLI
hTADG15 FVDAYENSNS TEFVSLASKV KDALKLLYSG VPFLGPYHKE SAVTAFSEGS 150
Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z Z
hTADG15 VIAYYWSEFS IPQHLVEEAE RVMAEERVVM LPPRARSLKS FVVTSVVAFP 200
mapranin
hTADG15 TDSKTVQRTQ DNSCSFGLHA RGVELMRFTT PGFPDSPYPA HARCQWALRG 250
mEpithin I-PRML H-AAVT NV
hTADG15 DADSVLSLTF RSFDLASCDE RGSDLVTVYN TLSPMEPHAL VQLCGTYPPS 300
mEpithinV-P HD SV -RFS
hTADG15 YNLTFHSSQN VLLITLITNT ERRHPGFEAT FFQLPRMSSC GGRLRKAQGT 350
mEpithinLF-V GL F-QLPRMSSC GGRLRRAQGT 350
hTADG15 FNSPYYPGHY PPNIDCTWNI EVPNNQHVKV SFKFFYLLEP GVPAGTCPKD 400 mEpithin -SN KRN RLVD- NV-S-T
hTADG15 YVEINGEKYC GERSOFVUTS NSWYTTERE GROOMER GROOMER
hTADG15 YVEINGEKYC GERSQFVVTS NSNKITVRFH SDQSYTDTGF LAEYLSYDSS 450 mEpithinGSSSHHN
hTADG15 DPCPGQFTCR TGRCIRKELR CDGWADCTDH SDELNCSCDA GHQFTCKNKF 500
mEpithinQ-
hTADG15 CKPLFWVCDS VNDCGDNSDE QGCSCPAQTF RCSNGKCLSK SQQCNGKDDC 550
mEpithin
hTADG15 GDGSDEASCP KVNVVTCTKH TYRCLNGLCL SKGNPECDGK EDCSDGSDEK 600
mEpithin T T
hTADG15 DCDCGLRSFT RQARVVGGTD ADEGEWPWQV SLHALGQGHI CGASLISPNW 650
mEpithin N KNLD-
hTADG15 LVSAAHCYID DRGFRYSDPT QWTAFLGLHD QSQRSAPGVQ ERRLKRIISE 700
mEpithinFQKN-KY- MLKSLKT-
hTADG15 PFFNDFTFDY DIALLELEKP AEYSSMVRPI CLPDASHVFP AGKALWVTGW 75000 (1)
mEpithin -SS VTVT
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MIADGIS GHIQIGGIGA LILQKGEIRV INQTICENLL POOTTPRMMC VGFT SCOTTES AND
سيلا عاميره ويلا المسترقي ومبارين
hTADG15 CQGDSGGPLS SVEADGRIFQ AGVVSWGDGC AQRNKPGVYT RLPLFRDWIK 850
mEpicnin
hTADG15 ENTGV* (SEQ ID No. 2)
mEpithin RAHWGIAAWT DSRPQTPTGM PDMHTWIQER NTDDIYAVAS PPQHNPDCEL
hTADG15
MELLITHE HP (SEC ID NO. 10)

FIGURE II

LOCUS HSU20428 2900 bp max DEFINITION Human SNC19 maxA sequence. 2900 bp 17-MAR-1997 mana 731 U20428 ACCESSION NID g1890631 KEYWORDS SOURCE human. ORGANISM Homo sapiens Eukaryotae: mitochondrial eukaryotes: Metazos: Chordsta: Vertebrata: Eutheria: Primates: Catarrini: Hominidae: Homo. 1 (bases 1 to 2900)
Zheng,S., Cai.X., Geng,L., Cao,J., Ineng,L. and Zhi,I.Z. SNC19 gene in Homo sapiens REFERENCE AUTHORS TITLE Unpublished 2 (bases 1 to 2900) JOURNAL REFERENCE Zheng, S.
Direct Submission AUTHORS TITLE

JOURNAL

Submitted (30-JAN-1995) Shu Zheng, Canter Institute, Thejiang Medical University, Hangzhou, 310009, Feoples Republic of China



					TΑ	DG15	: :	تج	iGA(CGC	CC.	TCG	GGG	TA	CCA	\TG	ggæ:	.:::	14.70	:033	cc:	:GC.	AGS	326	CAG:	3533	ccc	ددی	.GZ	CTT	CGG	CGCGGG	ACT	81
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